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Melphalan Tablets

» Melphalan Tablets contain not less than 90.0 percent and not more than 110.0 percent of the labeled amount of melphalan ($C_{13}H_{18}Cl_2N_2O_2$).

Packaging and storage—Preserve in well-closed, light-resistant, glass containers.

USP Reference standards ⟨11⟩—

USP Melphalan Hydrochloride RS

Identification—

A: The retention time of the major peak in the chromatogram of the *Assay preparation* corresponds to that in the chromatogram of the *Standard preparation,* as obtained in the *Assay.*

B: Shake a portion of finely powdered Tablets, equivalent to about 2 mg of melphalan, with 20 mL of alcohol, and filter: a 1-mL portion of the solution so obtained responds to *Identification* test *B* under *Melphalan*.

Dissolution ⟨711⟩—

Medium: 0.1 N hydrochloric acid; 900 mL.

Apparatus 2: 50 rpm.

Time: 30 minutes.

Determine the amount of $C_{13}H_{18}Cl_2N_2O_2$ dissolved by employing the following method.

Mobile phase—Transfer 2 grams of ammonium acetate, 2 mL of glacial acetic acid, and 0.4 mL of triethylamine to a suitable flask containing 1500 mL of water and 500 mL of acetonitrile. Stir until all solids are dissolved and well mixed, then filter and degas.

Chromatographic system (see *Chromatography ⟨621⟩*)—The liquid chromatograph is equipped with a 254-nm detector and a 4.6-mm × 5-cm column that contains packing L7. The flow rate is about 1.5 mL per minute. Chromatograph replicate injections of the Standard solution, and record the peak responses as directed for *Procedure:* the relative standard deviation is not more than 3.0%.

Procedure—Inject a volume (about 50 µL) of a filtered portion of the solution under test into the chromatograph, record the chromatogram, and measure the response for the major peak. Calculate the quantity of $C_{13}H_{18}Cl_2N_2O_2$ dissolved in comparison with a Standard solution having a known concentration of USP Melphalan Hydrochloride RS in the same *Medium* and similarly chromatographed.

Tolerances—Not less than 80% *(Q)* of the labeled amount of $C_{13}H_{18}Cl_2N_2O_2$ is dissolved in 30 minutes.

Uniformity of dosage units ⟨905⟩: meet the requirements.

Procedure for content uniformity—Place 1 Tablet in a 200-mL volumetric flask, add 10 mL of water and 10 mL of alcohol, sonicate to dissolve the soluble components in the mixture, dilute with alcohol to volume, mix, and filter to obtain a clear solution. Dissolve an accurately weighed quantity of USP Melphalan Hydrochloride RS in alcohol to obtain a Standard solution having a known concentration of about 10 µg per mL. Concomitantly determine the absorbances of the solution from the Tablet and the Standard solution in 1-cm cells at the wavelength of maximum absorbance at about 260 nm, with a suitable spectrophotometer, using alcohol as the blank. Calculate the quantity, in mg, of melphalan ($C_{13}H_{18}Cl_2N_2O_2$) in the Tablet taken by the formula:

$$(305.20/341.66)(T/D)C(A_U/A_S)$$

in which 305.20 and 341.66 are the molecular weights of melphalan and melphalan hydrochloride, respectively; T is the labeled quantity, in mg, of melphalan in the Tablet; D is the concentration, in µg per mL, of melphalan in the solution from the Tablet, on the basis of the labeled quantity per Tablet and the extent of dilution; C is the concentration, in µg per mL, of USP Melphalan Hydrochloride RS in the Standard solution; and A_U and A_S are the absorbances of the solution from the Tablet and the Standard solution, respectively.

Assay—

Mobile phase—Prepare a solution of 0.025 M diethylamine in a mixture of methanol and water (1:1), adjust with 3.5 N hydrochloric acid to a pH of 5.5, filter, and degas. Make adjustments if necessary (see *System Suitability* under *Chromatography ⟨621⟩*).

Standard preparation—Dissolve an accurately weighed quantity of USP Melphalan Hydrochloride RS in alcohol, and quantitatively dilute with alcohol to obtain a solution having a known concentration of about 0.9 mg of melphalan hydrochloride per mL. Pipet 10 mL of this solution into a 100-mL volumetric flask containing 75 mL of alcohol and 2.0 mL of glacial acetic acid, dilute with alcohol to volume, and mix to obtain

a *Standard preparation* having a known concentration of about 90 µg of USP Melphalan Hydrochloride RS per mL (equivalent to about 80 µg of melphalan per mL).

Assay preparation—Weigh and finely powder not fewer than 20 Tablets. Transfer an accurately weighed portion of the powder, equivalent to 8 mg of anhydrous melphalan, to a 100-mL volumetric flask. Add about 75 mL of alcohol and 2.0 mL of glacial acetic acid to the flask, and sonicate for 15 minutes. Cool, dilute with alcohol to volume, and mix. Filter through a medium-porosity, sintered-glass funnel, discarding the first few mL of the filtrate, and use the remainder of the filtrate as the *Assay preparation.*

Chromatographic system (see *Chromatography ⟨621⟩*)—The liquid chromatograph is equipped with a 254-nm detector and a 4.2-mm × 25-cm column that contains packing L7. The flow rate is about 1 mL per minute. Chromatograph the *Standard preparation,* and record the peak responses as directed for *Procedure:* the tailing factor for the analyte peak is not more than 2.0; and the relative standard deviation for replicate injections is not more than 2.0%.

Procedure—Separately inject equal volumes (between 10 and 20 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the quantity, in mg, of melphalan ($C_{13}H_{18}Cl_2N_2O_2$) in the portion of Tablets taken by the formula:

$$(305.20/341.67)(0.1C)(r_U/r_S)$$

in which 305.20 and 341.67 are the molecular weights of melphalan and melphalan hydrochloride, respectively; C is the concentration, in µg per mL, of melphalan hydrochloride in the *Standard preparation;* and r_U and r_S are the peak responses obtained from the *Assay preparation* and the *Standard preparation,* respectively.

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
MELPHALAN TABLETS	Documentary Standards Support	SM32020 Small Molecules 3
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM32020 Small Molecules 3

Chromatographic Database Information: Chromatographic Database

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